Effect of *Aficamten* on Structure and Function in Patients with Obstructive Hypertrophic Cardiomyopathy: The FOREST-HCM CMR Sub-study

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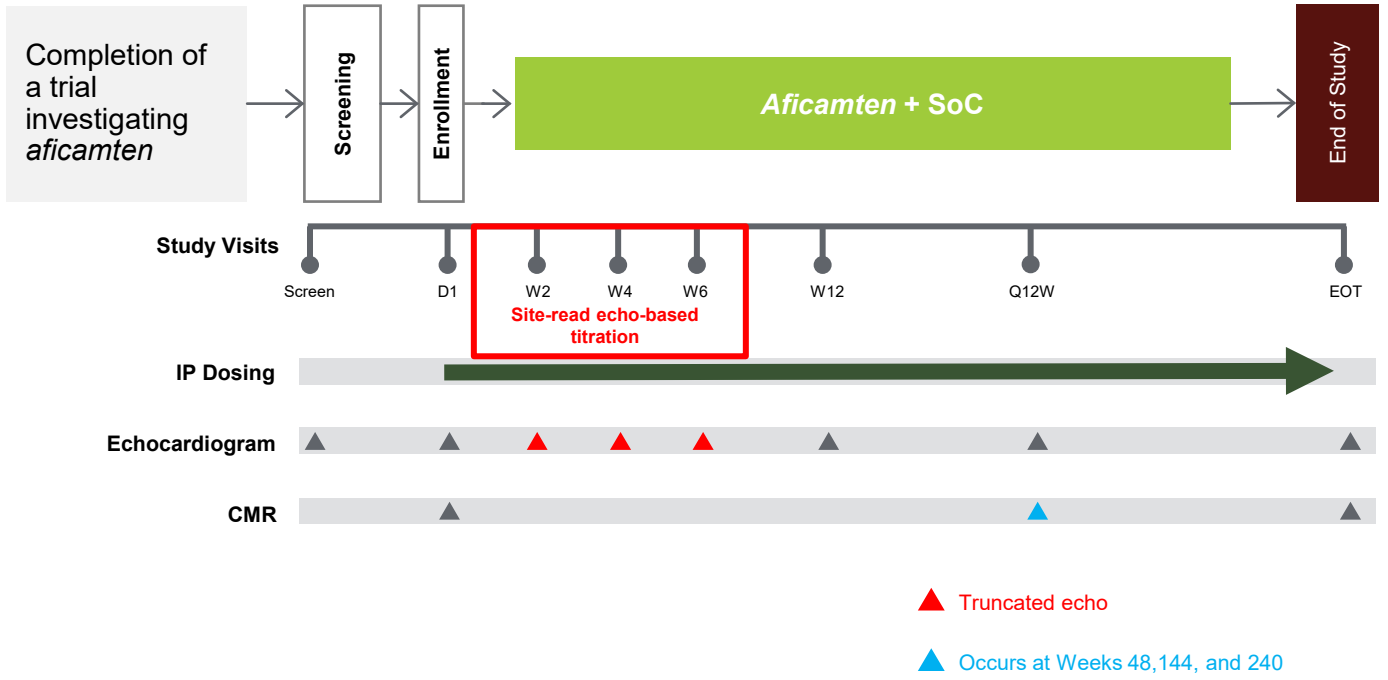
Disclosures

Dr. Masri: Consultant/advisor fees: Tenaya, Attralus, Cytokinetics, Bristol Myers Squibb, Eidos, Pfizer, Haya, Lexion, BioMarin, Alexion, and Ionis; research grants: Ionis, Pfizer, Cytokinetics, and Attralus.

Dr. Cardoso: Research support: Modest and Cleerly. **Dr. Abraham:** Research grants: Cytokinetics and MyoKardia. **Dr. Choudhury:** No disclosures to report. **Dr. Rader:** Speaker bureau fees: Bristol Myers Squibb and Medtronic; consultant/advisor fees: Bristol Myers Squibb, Cytokinetics, ReCor, and Medtronic. **Dr. Saberi:** Consultant/advisor fees: Bristol Myers Squibb; research grants: Bristol Myers Squibb, Cytokinetics, Novartis, and Actelion Pharmaceuticals. **Dr. Tower-Rader:** Research grants: Cytokinetics and Bristol Myers Squibb. **Dr. Wang:** Consultant/advisor fees: Cytokinetics, Bristol Myers Squibb, and BioMarin; grants or grants pending: Cytokinetics, Bristol Myers Squibb, and Abbott Vascular; royalties for serving as an editor: UpToDate; payment for development of educational presentations: the American College of Cardiology Foundation. **Drs. Heitner, Kupfer, Malik, Melloni, Wei,** and **Ms. Wohltman:** Employees and stockholders: Cytokinetics. **Dr. Kwong:** Grants: the National Heart, Lung, and Blood Institute, Bristol Myers Squibb, Cytokinetics, and Alnylam.

Background and Methods

- *Aficamten* is a next-in-class cardiac myosin inhibitor in development for the treatment of HCM.
- FOREST-HCM (NCT04848506) is an open-label extension study of *aficamten* in patients with HCM, with an optional CMR sub-study.
- Between May 2021 and August 2023, 117 patients with obstructive HCM were enrolled in FOREST-HCM. By August 15 (data cut-off), 42 patients had opted to participate in the CMR sub-study and 16 had completed both baseline and Week 48 studies (1 year).
- LGE was defined as areas of signal intensity ≥6 SDs from normal myocardium and was expressed as the percentage of total left-ventricular myocardial mass (LGE%).



HCM: hypertrophic cardiomyopathy; CMR: cardiac magnetic resonance imaging; LGE: Late gadolinium enhancement

Baseline Characteristics

Characteristic	All oHCM patients (N=117)	CMR cohort (n=16)
Age, years, mean (SD) [range]	60.3 (13.7) [23-84]	61.3 (15.26) [23-78]
Female, n (%)	55 (47.0)	10 (62.5)
Race, %, White/Black/Asian/Other	96/2/1/2	94/0/6/0
BMI, kg/m^2, mean (SD) [range]	29.4 (4.7) [20-51]	29.0 (4.5) [24-40]
NYHA class, n (%)		
Class II	63 (53.8)	11 (68.8)
Class III	54 (46.2)	5 (31.3)
Family history of HCM, n (%)	27 (23.1)	2 (12.5)
Time from HCM diagnosis, years, mean (SD) [range]	6.9 (7.0) [1-47]	3.9 (4.42) [1-19]
Beta-blocker, n (%)	95 (81.2)	15 (93.8)
Calcium channel blocker, n (%)	16 (13.7)	2 (12.5)
Disopyramide, n (%)	22 (18.8)	4 (25)

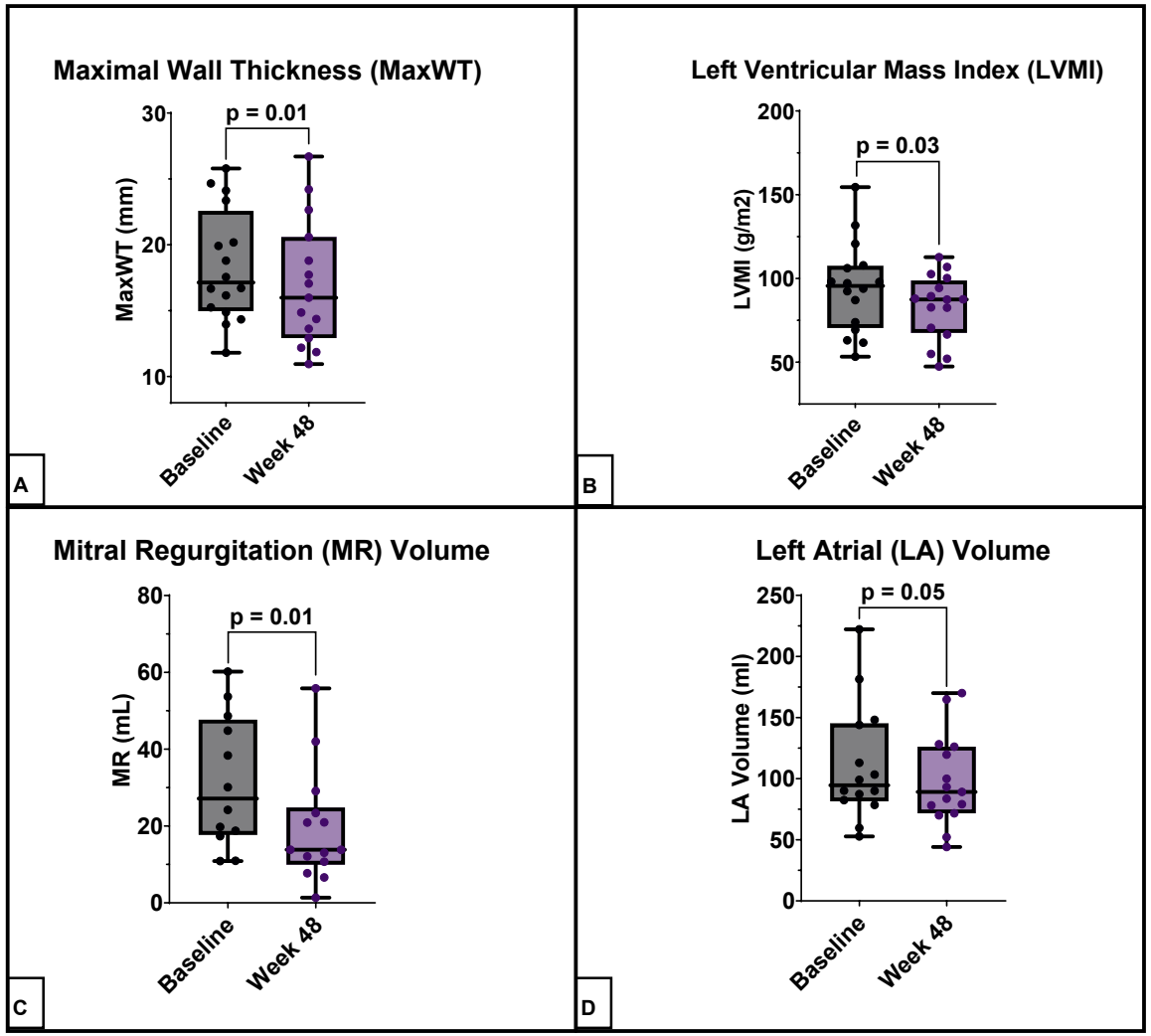
Hemodynamic, Biomarker, and Clinical Changes in the Overall Population and CMR Subgroup over 48 Weeks of *Aficamten* Treatment

Characteristic	All oHCM patients N=117				CMR cohort N=16			
	Baseline	Week 48	Δ	*P* value	Baseline	Week 48	Δ	*P* value
LVEF, %^	68.2 ± 5.6	64.2 ± 5.4	-4.9 ± 6.0	<0.0001	67.2 ± 4.7	63.3 ± 5.7	-3.9 ± 5.6	0.014
Resting LVOT-G, mmHg ^	57.0 ± 33.0	13.5 ± 13.8	-38.3 ± 33.7	<0.0001	50.1 ± 28.2	13.1 ± 10.4	-37 ± 27	<0.0001
Valsalva LVOT-G, mmHg ^	91.5 ± 37.9	29.9 ± 23.9	-51.8 ± 36.6	<0.0001	86.9 ± 26.0	26.5 ± 23.5	-60 ± 30	<0.0001
NT-proBNP, pg/mL*	851 (352, 1921)	110 (59, 231)	-425 (-1292, -144)	<0.0001	530 (295, 1775)	131 (78, 207)	-377 (-1292, -206)	<0.0001
hs-Trop I, ng/L*	11.2 (5.1, 19.8)	5.6 (3.5, 12.5)	-3.1 (-8.1, 0.0)	0.0002	8.1 (4.7, 12)	5.5 (3.5, 12.5)	-1.6 (-6.4, 0.0)	0.1
KCCQ-CSS ^	69.9 ± 20.1	87.4 ± 13.6	14.4 ± 14.4	<0.0001	75.8 ± 18.4	86.9 ± 12.9	11.1 ± 11.0	0.0011
NYHA class, n (%)								
Class I	0	24 (54)	–	–	0	8 (50)	–	–
Class II	63 (54)	18 (41)			11 (69)	7 (44)		
Class III	54 (46)	2 (5)			5 (31)	1 (6)		

^Mean (SD), * Median (Interquartile Range)

Cardiac Structure on CMR at Baseline and Week 48

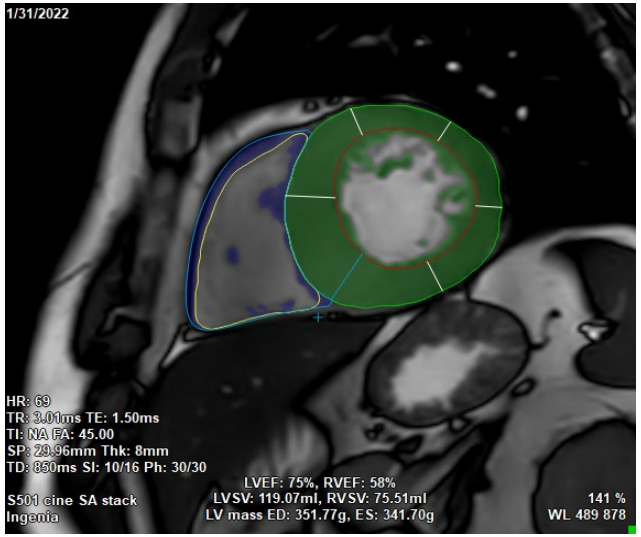
Variable	Change from baseline	*P* value
LVMI, g/m²	-11.4 ± 19.4	0.03
Max WT, mm	-1.3 ± 1.8	0.02
LAV, mL	-16.3 ± 26.4	0.05
MR volume, mL	-12.9 ± 15.1	0.01
MR fraction, %	-9.5 ± 15.1	0.05
LV global mass of LGE, g	-0.6 ± 5.0	0.64
Native T1, ms	16.0 ± 135.2	0.64
Global ECV, %	-0.4 ± 2.4	0.56

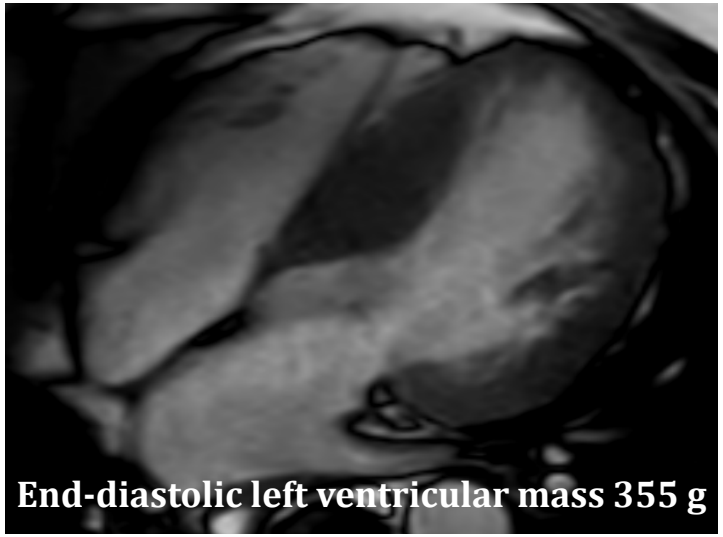


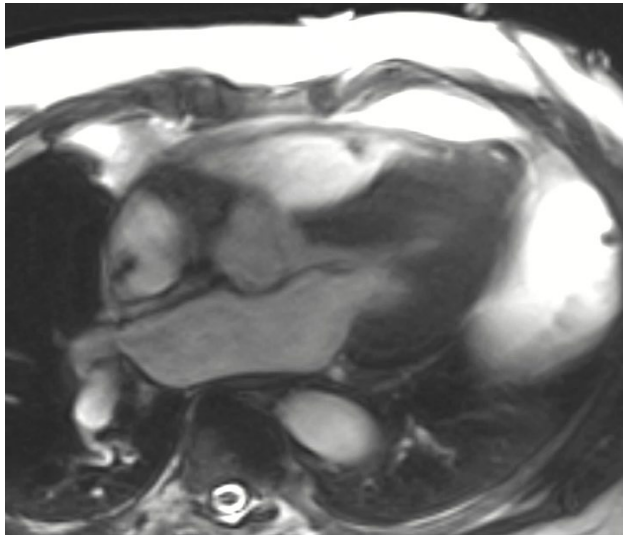
Patient 1

Patient 2

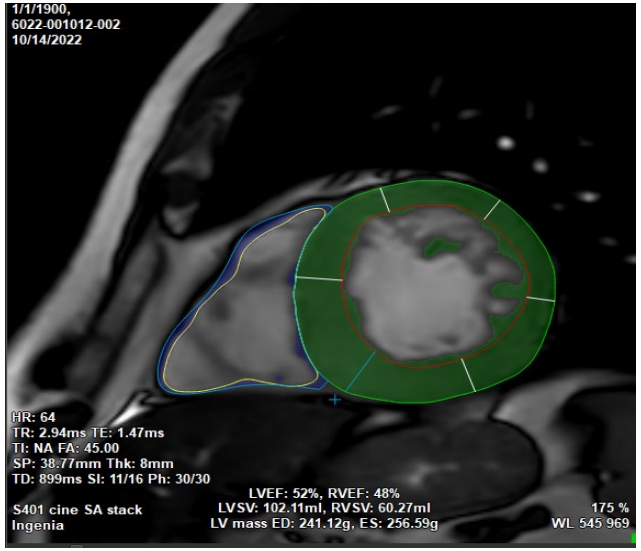
Baseline

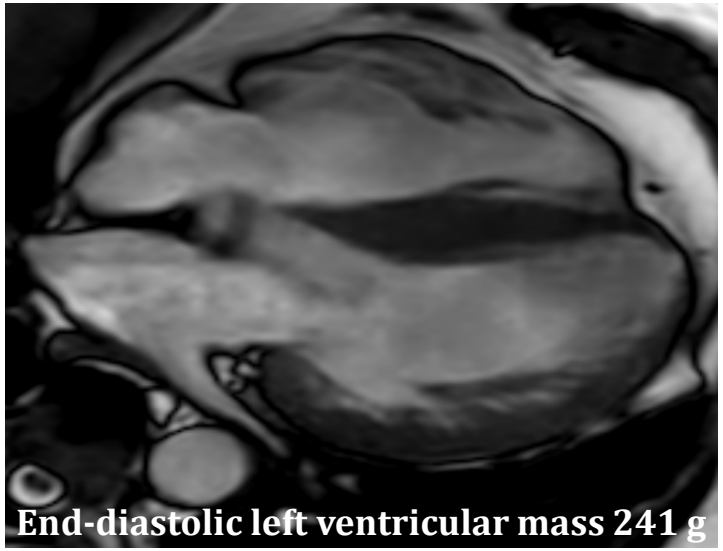


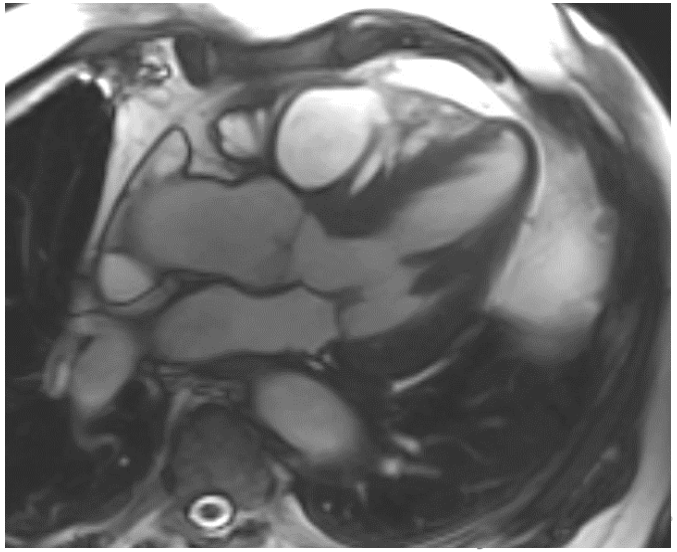




48 weeks







Conclusions

- *Aficamten* treatment for 1 year resulted in:
  1. Favorable cardiac structural remodeling
  2. Reduced mitral regurgitation quantitatively
  3. Stable interstitial and replacement myocardial fibrosis

- The 5-year CMR sub-study of FOREST-HCM is ongoing and will continue to evaluate the effects of *aficamten* as a potential disease-modifying agent in HCM